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ATTORNEY'S DOCKET NO: C01039.70077.US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Arthur M. Krieg

Serial No:

Not Yet Assigned

Filed:

July 14, 2003

For:

IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES

Examiner:

Not Yet Assigned

Art Unit:

Not yet Assigned

Mail Stop Patent Application Commissioner for Patents P.O. Box 1450 Alexandria, VA 02213-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed before the mailing of a First Office Action on the merits, and therefore, no fee is enclosed herewith.

PART II: Information Cited

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

The Applicants hereby make the following additional information of record in the above-identified application:

The following are related pending U.S. non-provisional applications which do not appear on the 1449 form.

Serial No.		Filing Date
08/386,063		02/07/95
08/738,652		10/30/96
08/960,774		10/30/97
09/030,701		02/25/98
09/082,649	•	05/20/98
09/146,072		09/02/98
09/154,614		09/16/98
09/191,170	•	11/13/98
09/241,653		02/02/99
09/286,098		04/02/99
09/306,281		05/06/99
09/316,199		05/21/99
09/325,193	j.	06/03/99
09/337,619		06/21/99
. 09/337,893		06/21/99
09/361,575		07/27/99

The following are related PCT Publications, published after the priority date (copies were provided in priority application):

WO 98/37919		09/03/98
WO 98/18810		05/07/98
WO 98/40100		09/17/98
WO 98/52581	,	11/26/98

The following are remarks concerning the other information cited:

PART III: Remarks

Documents cited on the attached form PTO-1449 (modified) are enclosed unless otherwise indicated on the attached form PTO-1449 (modified). It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

- 2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
- 3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,

By:

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Docket No. C01039.70077.US

Dated: July 14, 2003

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FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT APPLICANT Krieg FILING DATE July14, 2003 SERIAL NO Not Yet Assigned ROUP Not Yet Assigned

U.S. PATENT DOCUMENTS

Exam Init	Ref Des	Document No.	Date	Name -	Class	Sub Class	FILING DATE If Appropriate
*		3,906,092	09/16/75	Hilleman et al.			
*	1	5,248,670	09/28/93	Draper et al.	514	44	
*		5,585,479	12/17/96	Hoke et al.	536	24.5	
*		5,663,153	09/02/97	Hutcherson et al.	514	44	
*		5,723,335	03/03/98	Hutcherson et al.	435	375	
*		5,786,189	07/28/98	Locht et al.	435	172.3	
*		5,849,719	12/15/98	Carson et al.	-514	44	
*		6,498,148	12/24/02	Raz	1.	, , , ,	

FOREIGN PATENT DOCUMENTS

		Country & Pub.			1	Sub	Translation	
		Doc. No. (11)	Date (43)		Class	Class	Yes	No
*		WO 91/12811	09/05/91	PCT	A61K	31/70		
*		0468520 A3	01/29/92	EPO	A61K	31/70		
*		WO 92/03456	03/05/92	PCT	C07H	15/12		
*	1	WO 92/18522	10/29/92	PCT	C07H	21/00		10
*		WO 92/21353	12/10/92	PCT	A61K	31/70		-
*	1	0302758 81	03/16/94	EPO	C12N	15/37		
*	-	WO 94/19945	09/15/94	PCT	AOIN	43/04		
*	1	WO 95/05853	03/02/95	Regents of the University of CA				
*		WO 95/26204	10/95	PCT	A61K	48/00		-
*		WO 96/02555	02/01/96	PCT				
*		WO 96/35782	11/14/96	Applied Research Systems				
*		WO 97/28259	08/07/97	PCT	C12N	15/00		
*	1	WO 98/18810	05/07/98	PCT	C07H	21/00		
*		WO 98/37919	09/03/98	PCT	A61K	49/00		
*	1	WO 98/40100	09/17/98	PCT	A61K	39/39	-	
*		WO 98/52581	11/26/98	PCT	A61K	35/00		-
*	 	WO 98/14210	04/09/98	PCT .	A61K	39/35		

FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO.	SERIAL NO	
		C01039.70077.US	Not Yet Assigned	
			APPLICANT Krieg	:
			FILING DATE July14, 2003	GROUP Not Yet Assigned
*	WO 98/16247	04/23/98	Regents of the University of CA	
*	WO 98/32462	07/30/98	Wagner et al.	
*	WO 98/49288	11/05/98	Hybridon, Inc.	
*	WO 98/55495	12/10/98	Dynavax Technologies Corp.	
*	WO 99/11275	03/11/99	Regents of the University of CA	
	<u> </u>	.L		
*	Adya N et al., Exp	oansion of CRI	OTHER ART Title, Date, Pertinent Pages, Public B's DNA recognition specificity by Tage conserved DNA-binding domain of Cl	x results from interaction with Ala-Ala-
	91(12):5642-6,7	Jun 1994.		
*	Angier, N., Micro	be DNA Seen	as Alien By Immune System, New York	Times, 4111195
*		Major Immedi	y of a Phosphorothioate Oligonucleotide ate-Early Region. <i>Antimicrobial Agents</i>	Complementary to RNA of the Human and Chemotherapy, 37:1945-1954,
*		ical and Immur	nological Studies on Cellular Componen	ts of Tubercle Bacilli, Kekkaku, Vol.
*	and bacterial DNA	A. J Immunol 1	Cactivity in murine and human cells by 57(5).1840-5, 1996.	
*		Myelogenous le	eukemia and Myelodysplastic Syndrome	otide with a Sequence Complementary :: Initial Results of a Phase I Trial,
*			to human leukocytes. Evidence for a re	
*	Berg DJ et al., Int	erleukin-10 is	of DNA. J Clin Invest 76(6):2182-90, 19 a central regulator of the response to LP to not endotoxin tolerance. J Clin Invest 9	S in murine models of endotoxic shock
*		al., Interferon-	gamma induction by lipopolysaccharide	
*	Blaxter et al., Ger Parasitology, 77:	ies expressed i 77-93.	n Brugia malayi infective third stage lar	
*	Antisense Nucleic	Acid Drug De	n and modulation of immune stimulation ν 7(5):461-71, Oct 1997.	
*	Med 128(3):329-3	38, Šep 1996.		oate oligodeoxynucleotides. J. Lab Clin
*	Biochemical Phar	mącology, Vo	on by an Antisense Oligomer Compleme 1. 45, 10:2037-2043, 1993.	
*	Mol Cell Biol 10(1):422-5, Jan 1		
*	Chace, J. et al., R. Immunopathology		fferentiation in CD5+ and Conventional 327-332.	B Cells, Clinical Immunology and

FORM	и РТО	-1449 (Modified)	ATTY. DOCKET NO.	SERIAL NO
	LICAT	OF PATENTS AND IONS FOR APPLICANT'S IATION DISCLOSURE	C01039.70077.US	Not Yet Assigned
11 (STATEMENT		0
	,		APPLICANT Krieg	
	7.		FILING DATE July14, 2003	GROUP Not Yet Assigned
*			c series I repeats in the simian cytomego pasal enhancers and cyclic AMP respons	
*		Chu RS et al., CpG oligodeoxym Med 186(10):1623-31, 17 Nov 1		
*	16	lipopolysaccharides. J Immunol	156(12):4570-5, 15 Jun 1996.	ma in vivo and increases the toxicity of
*	-	Member of the GCGGGGGCG (es Gene FGFI-C Encodes a Zinc Finger GSG) Element-Binding Protein Family.	Mol. Cell. Biol., 2:3835-3841, 1991.
*		Crystal, Transfer of Genes to Hu 1995.	mans. Early Lessons and Obstacles to S	uccess. Science, Vol. 270, pp. 404-410,
*			(1L-10) inhibits human lymphocyte int mulatory factor/IL-12 synthesis in acces	
*		Englisch et al., Chemically Mod 30:613-629, 1991.	fied Oligonucleotides as Probes and Inh	nibitors, Angew. Chem. Int. Ed. Engl.,
* *		allergen- induced airway eosinor	vith Mycobacterium bovis-Bacillus Calm philia. <i>J Exp Med</i> 187(4):561-9, 16 Feb	1998.
*	· ·			nunology Today, Vol. 13, 2:52-55, 1992.
*		Abstract No. 182630 (April 29,		
*		Research, 14(13):5399, 1986.	f DNA via deoxynucleotide H-phosphor	nate intermediates, <i>Nucleic Acid</i>
*			g Pains. Science (1995), 270:575-576.	
′*		Hadden J et al., Immunostimular		
*		Hadden J et al., Immunopharmac	cology, JAMA, (1992) 268:20:2964-296	9.
*		interleukin-12 and tumor necrosi	A induces murine interferon-gamma pros s factor-alpha. Cell Immunol 167(1):72-	-8, 1996.
.*		Growth Factor β1 or Rb Oligonu	man Hematopoietic Progenitors from Qucleotides, <i>J. Exp. Med.</i> , (1991) 174:925	-929.
*		L	the Murkier. Biotechnology, 12:828, Au	
*	•		of multiple nuclear factors that interact value of the factor of the fac	
*	7	TGACGTCA abolishes specific 1989.	<u> </u>	activation. Genes Dev 3(5):612-9, May
*		Human Immunodeficiency Virus Infusion", Antisense Research as	Type I in the Adult male Rate Followind Development, (1994), 4:43-52	0.
*		Ishikawa R et al., IFN induction 150(9):3713-27, 1 May 1993	and associated changes in splenic leuko	cyte distribution. J Immunol

FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		ATTY. DOCKET NO.	SERIAL NO			
		C01039.70077.US	Not Yet Assigned			
		APPLICANT Krieg				
		FILING DATE July14, 2003	GROUP Not Yet Assigned			
*	Jakway JP et al., Growth regulati	on of the B lymphoma cell line WEHI-2.				
	lipopolysaccharide, and other bac	cterial products. J Immunol 137(7):2225-	31, 1 Oct 1986.			
*	50, 1991.	ellular uptake of antisense oligonucleotic				
*	Proteins of Mycobacterium bovis	ivity of Synthetic Oligonucleotides with BCG, <i>Jpn. J. Cancer Res.</i> , 83:244, 1992				
*		oguanylate to Scavenger Receptors is Renduce IFN, <i>J. Biochem.</i> , Vol. 116, 5:991-				
* .		nucleotides are effective in prevention of				
*		on by CpG oligonucleotides. Conversion	of a Th2 response to a Th1 response			
*		tides can reverse as well as prevent Th2-1	nediated inflammation in a murine			
*	Klinman DM et al., CpG motifs	oresent in bacteria DNA rapidly induce lynma. <i>Proc Natl Acad Sci USA</i> 93(7):287				
*	Krajewski, W., et al., "A Monon	neric Derivative of the Cellular Trnscriptional ar and Cellular Biology, 14:11:7204-721	on Factor CREB Functions as a			
*		fense mechanism based on the recognition				
*		deoxyribonucleotides by lymphoid cells i	s heterogeneous and inducible.			
*	Krieg AM et al., Oligodeoxynuc	leotide modifications determine the magn	itude of B cell stimulation by CpG			
*	Krieg AM et al., "Modification of	motifs. Antisense Nucleic Acid Drug Dev 6(2):133-9, Summer 1996. Krieg AM et al., "Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholesteryl moiety increases cellular association and improves efficacy", Proc. Natl. Acad. Sci., (1993), 90:1048-1052				
*		Pathogenic Factor in Systemic Lupus Ery				
*		ate Oligodeoxynucleotides: Antisense or A	Anti-Protein?, Antisense Research and			
*		mulation by Oligodeoxynucleotides", App	olied Antisense Oligonucleotide			
*		pacterial DNA trigger direct B-cell activat	tion. Nature 374:546-9, 1995.			
*	Krieg AM et al, "The role of Cp Jan 1998.	G dinuleotides in DNA vaccines", Trend	ls in Microbiology, Vol. 6, pp. 23-27,			
*		dogenous Retroviral Sequences in the Re	gulation of Lymphocyte Activation,			
*	Kuramoto et al., Oligonucleotide 83:1128-1131, November 1992.	Sequences Required for Natural Killer C	Cell Activation, Jpn. J. Cancer Res.,			
*	Kwok, R., et al., "Nuclear protein (1994)	n CBP is a coactivator for the transcription	on factor CREB", Nature, 370:223-226,			
*	Lacour, J., Clinical Trials Using	Polyadenylic-Polyuridylic Acid as an Adesponse Modifiers, 4(5):538, 1985.	juvant to Surgery in Treating Different			

FORM	PTO-1449 (Modified)	ATTY. DOCKET NO.	SERIAL NO
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S		C01039.70077.US	Not Yet Assigned
INI	FORMATION DISCLOSURE STATEMENT		
		APPLICANT Krieg	
		FILING DATE July14, 2003	GROUP Not Yet Assigned
*	1174:221-233, (1993)	egulation by CREB and its relatives", Bio	
*	d(CGCGAATT(08A)GCG). Bid	Guanine 8-Oxoadenine Base Pairs in the Cochemistry, 31(36):8415-8420, 1992.	
*		ntagonism of immunostimulatory CpG-olated compounds. <i>J Immunol</i> 160(3):1122-	
*	Mastrangelo et al. Seminars in O	ncology. Vol. 23, 1:4-21, 1996.	
*	Matson S and Krieg AM, Nonspoligonucleotides. Antisense Res	ecific suppression of [3H]thymidine incor Dev 2(4):325-30, Winter 1992.	poration by "control"
*		e phosphorothioate oligonucleotid	
	Antisense Res Dev 3(4):309	appa B p65 causes sequence-speci 0-22. Winter 1993.	inc immune stimulation.
*	Messina et al., The Influence of	DNA Structure on the <i>in vitro</i> Stimulation tigens. Cellular Immunology, 147:148-1:	
*		vitro Murine Lymphocyte Proliferation by	
*		on of a Phosphorothioate Oligonucleotide nune Effect in vivo in a Sequence-Specific 130-136	
*	translationally regulated during t	elated protein kinase from leishmania mex he life cycle. <i>J. Biol. Chem.</i> 268:28, 2104	
*	New England BIOLABS 1988	-1989 Catalog	
*	Nyce JW and Metzger WJ, DNA 1997.	antisense therapy for asthma in an anima	ll model. Nature 385:721-725, 20 Feb
*		n Vitro Selection of DNA Elements Highlascriptional Activator, Tax, Molecular and	
*	Pisetsky, D., "Stimulation of in v Molecular Biology Repairs, (19	vitro proliferation of murine lymphocytes 93) 18:217-221	by synthetic oligodeoxynucleotides",
*	Pisetsky et al., Stimulation of M	urine Lymphocyte Proliferation by a Phos mplex Virus. <i>Life Science</i> , Vol. 54, pp. 1	
*		operties of DNA, The Journal of Immuno	
*	Pisetsky, Immunological Consec 225 (1995).	uences of Nucleic Acid Therapy, Antisen	se Research and Development, 5:219-
*	Raz E et al., Preferential induction	on of a Th1 immune response and inhibiti Proc Natl Acad Sci USA 93(10):5141-5,	
*		tory DNA sequences function as T helper	
*		oxicological Effects of rel A Antisense Phoment, 4:99-107, (1994)	osphorothioates in CD-1 Mice",
*	Sato et al., Immunostimulatory I Science, Vol. 273, pp. 352-354,	DNA Sequences Necessary for Effective I	ntradermal Gene Immunization,

FORM	M PTO-1449 (Modified)	ATTY. DOCKET NO.	SERIAL NO
	LIST OF PATENTS AN LICATIONS FOR APPLI IFORMATION DISCLOS STATEMENT	CANT'S	Not Yet Assigned
	STATIENTEN	APPLICANT Krieg	
		FILING DATE July14, 2	2003 GROUP Not Yet Assigned
*	Schnell et al. Identi	ication and characterization of a Saccharom	
		elators. Eur. J. Biochem., 200:487-493.	yees core iside gone (1711(1) comerting
*	tract. Am J Physiol 2	67(5 Pt 1):L609-17, 1994.	luced inflammation in the lower respiratory
*	Schwartz DA et al., 152(2):603-8, 1995.	The role of endotoxin in grain dust-induced	lung disease. Am J Respir Crit Care Med
*	Invest 100(1):68-73		
*	. 275(5296):77-9, 3 J		
*		Macrophages sense pathogens via DNA mot d shock. Eur J Immunol 27(7):1671-9, Jul 1	
*	Stein CA et al., Olig 1988.	onucleotides as inhibitors of gene expression	n: a review. Cancer Research, 48:2659-2668,
*	Stull et al., Antigene Res., Vol. 12, 4:465		gs: Progress and Prospects, Pharmaceutical
*	Subramanian et al.,	Theoretical Considerations on the "Spine of cG) d(GCGCTTAAGCGC): Monte Carlo Co	Hydration" in the Minor Groove of omputer Simulation. <i>Proc. Nat'l. Acad. Sci.</i>
*	. Tanaka T et al., An	antisense Oligonucleotide complementary to	a sequence in IG2b increases G2b germline oglobulin secretion. <i>J. Exp. Med.</i> , 175:597-607,
*	Thorne PS., Experir Med 25(1):109-12,		wet and dry aerosolization techniques. Am J Ind
*	Tokunaga T et al., S	ynthetic Oligonucleotides with Particular Baerium bovis BCG Induce Interferons and Ac	
*	Tokunaga et al., A S	ynthetic Single-Stranded DNA, Ply (dG, dC ity and Suppresses Tumor Growth. <i>Jpn. J. C</i>	
*	Tsukada, J., et al., "	Franscriptional Factors NF-IL6 and CREB R in 1β Gene", <i>Molecular and Cellular Biolog</i>	Recognize a Common Essential Site in the
*			c Principle. Chemical Reviews, 90:543-584,
*	Wagner RW, Gene	nhibition using antisense oligodeoxynucleot	ides. Nature, 372:L333-335, 1994.
*	Wallace et al., Oligo 152:432-442 (1987)	•	nbinant DNA libraries. Methods in Enzymology,
*			rom reverse genetics. Science, 139:108-109,
*	Whalen R, DNA Va 3:168-175, 1996.	ccines for Emerging Infection Diseases: Wh	at If?, Emerging Infectious Disease, Vol. 2,
*		otor-mediated gene delivery and expression	in vivo. J. Biol. Chem., 263:14621-14624, 1988.
*	Wu-Pong S., Oligor 18:102-114, 1994.	ucleotides: Opportunities for Drug Therapy	and Research. Pharmaceutical Technology,

FORM	M PTO-1449 (Modified)	ATTY. DOCKET NO.	SERIAL NO			
-	LIST OF PATENTS AND LICATIONS FOR APPLICANT NFORMATION DISCLOSURE STATEMENT	C01039.70077.US	Not Yet Assigned			
	STATEMENT	APPLICANT Krieg				
		FILING DATE July14, 2003	GROUP Not Yet Assigned			
*		n bacteria, but not from vertebrates, induc h. Microbiol Immunol 36(9):983-97, 199	ces interferons, activates natural killer			
*		gmentation of natural killer cell activity ucleic acid fraction from <i>Mycobacterium</i>	and production of interferon-alpha/beta bovis BCG. Jpn J Cancer Res 79:866-73,			
*	Yamamoto S., Mode of Action Kekkaku, Vol. 69, 9:29-32, 1	Yamamoto S., Mode of Action of Oligonucleotide Fraction Extracted from Mycobacterium bovis BCG, Kekkaku, Vol. 69, 9:29-32, 1994.				
*		Yamamoto S et al., Unique Palindromic Sequences in Synthetic Oligonucleotides are Required to Induce INF and Augment INF-Mediated Natural Killer Activity. <i>J. Immunol.</i> , Vol. 148, 12:4072-4076, June 15, 1992.				
*	Yamamoto T et al., Ability o	Yamamoto T et al., Ability of Oligonucleotides with Certain Palindromes to Induce Interferon Production and Augment Natural Killer Cell Activity is Associated with Their Base Length. <i>Antisense Res. and Devel.</i> , 4:119-				
*			Having a Palindromic Sequence AACGTT Iler Activity. <i>Microbiol. Immunol.</i> , Vol.			
*		Oligonucleotides with Certain Palindron uphocytes in vitro. Jpn. J. Cancer Res., 8				
*	Yi, Ae-Kyung et al., IFN-γ P		onse to CpG Motifs in Bacterial DNA and			
*		Yi, Ae-Kyung et al., Rapid Immune Activation by CpG Motifs in Bacterial DNA, The Journal of Immunology,				
*	Zelphati, O. et al., Inhibition	of HIV-1 Replication in Cultured Cells womes, Antisense Res. and Devl., 3:323, 1				
*		oligonucleotide uptake in murine bone ma				
*	Zhao Q et al., Comparison of	cellular binding and uptake of antisense prethylphosphonate oligonucleotides. Ant	phosphodiester, phosphorothioate, and isense Res Dev 3(1):53-66, Spring 1993.			

* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 08/738,652, filed October 30, 1996, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

EXAMINER	 DATE CONSIDERED	7

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.

^{*} a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 09/337,636, filed June 21, 1999, and relied upon for an earlier filing date under 35 USC 120.